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VITAMIN A: AN URGENT NUTRITIONAL NEED FOR THE WORLD'S CHILDREN

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U.S. HOUSE OF REPRESENTATIVES

STAFF REPORT

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LETTER OF TRANSMITTAL

HOUSE OF REPRESENTATIVES,
SELECT COMMITTEE ON HUNGER,
Washington, DC, June 19, 1985.

To: Members of the Select Committee on Hunger.
From: Mickey Leland, Chairman.

I am pleased to transmit to Committee members the enclosed staff report "Vitamin A: An Urgent Nutritional Need for The World's Children." The report was prepared by Mary Ruth Herbers of the Majority staff. Minority staff consulted in the final preparation of the report. I wish to thank John Costello of Helen Keller International, Keith West of Johns Hopkins University, and John McKigney of the Agency for International Development for their assistance in preparing the report; they are not responsible for any errors.

I believe that this study highlights the opportunity to significantly reduce child blindness and death through vitamin A programs. This resource should be useful to the Committee in its work on international nutrition and hunger issues.

Sincerely,

MICKEY LELAND, *Chairman.*

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INTRODUCTION

Since its inception, the Select Committee on Hunger has been concerned with the link between malnutrition and childhood death rates in less developed countries. Recently, the committee learned of vital new evidence of this link: the provision of vitamin A supplements to children in less developed countries can reduce childhood mortality by 25 to 35 percent.

This crucial finding has dramatic implications for improving the lives of children worldwide. Most of the 40,000 persons who die daily throughout the world are children under the age of 5, who succumb to the combined effects of malnutrition and infection. Nutrition interventions can break this deadly cycle and have the possibility of alleviating sickness, reducing death rates, and improving the quality of life for those affected.

Nowhere is the opportunity to improve life and nutritional health more clearly illustrated than in the example of vitamin A intervention programs. This report discusses vitamin A therapy within the context of international health and nutrition strategies. The report: (I.) outlines the problem, extent, indicators, and consequences of vitamin A deficiency, (II.) describes the effectiveness of vitamin A therapy, and (III.) discusses enhancement of vitamin A programs through the Agency for International Development and private voluntary organizations (PVO's).

I. VITAMIN A DEFICIENCY—AN ANALYSIS

The problem

In a hearing before the Select Committee on Hunger on May 16, 1985, Dr. Alfred Sommer of Johns Hopkins University described vitamin A deficiency as a major cause of childhood morbidity and mortality. Following are excerpts from his testimony:

> Vitamin A deficiency is extremely common throughout the developing world. At least 5 to 10 million children develop nightblindness and other eye manifestations of vitamin A deficiency every year, and in Asia alone a quarter million of these children go blind. The number of children with subclinical vitamin A deficiency, who suffer other adverse effects, but do not have obvious ocular manifestations of the disease, probably reaches 20 million children throughout Asia, Africa, and Latin America.
>
> The earliest studies on children with inadequate dietary vitamin A suggested that vitamin A deficiency was important for general health and resistance to infection. Those observations were largely forgotten, being overshadowed by the dramatic changes observed in the eye.
>
> Recent studies in Indonesia indicate the impact of subclinical vitamin A deficiency on childhood survival may well be a far greater problem than changes in the eye. The first study, in which 4,000 children were followed for 18 months during 1977–78, demonstrated that those children with very early, mild eye changes died at four to twelve times the rate of otherwise identical children who did not have early eye changes. Evaluation of the survivors showed that the reason for increased mortality among children with eye signs of vitamin A deficiency was probably increased risks of respiratory disease and diarrhea. * * *

These findings indicate that vitamin A therapy, which has been used to prevent blindness for many years, may also save lives. (This is further substantiated by findings of a larger scale study discussed under Prevention.) Dr. Sommer theorizes that vitamin A is apparently necessary for healthy mucous membrane, the surface linings of the respiratory, urinary, and intestinal tracts which are the major areas where bacteria can enter the body.

When there is not enough vitamin A in the diet, these membranes change, and are no longer able to defend the body from bacteria. Therefore, in children who receive too little vitamin A, bacteria can grow more easily and the children suffer from more infections in lungs, kidneys, and gastrointestinal organs, leading to much higher death rates.

The extent

For years, it was known that vitamin A deficiency was a widespread problem. However, only in the last 20 years has it been considered a problem of major public health significance. An estimated 500,000 children are blinded every year from the vitamin A deficiency disease know as xerophthalmia. The World Health Organization (WHO) cites vitamin A deficiency as a current public health problem in 73 countries and territories.

The problem is most severe in Asia, Africa, and certain areas in South and Central America. In a 1983 study on Research Priorities for the Prevention of Blindness in Developing Countries published by Helen Keller International, the prevalence of xerophthalmia was described. The report states that in Indonesia, India, Bangladesh, and the Philippines, xerophthalmia is widespread. It is recognized as a problem, but not well delineated, in China, Malaysia, and Southeast Asia. The disease occurs to a lesser extent in Haiti, Central and South America, and the South Pacific. The magnitude of the problem in Africa is unknown but it is thought to be enormous.

Preschool-age children suffer the greatest effects of vitamin A deficiency. Many of them are blinded for life. A hospital-based study conducted in 1968 found that 75 percent of those treated for severe vitamin A deficiency who survived remained totally or partially blind.

The indicators

Young children are the most severely affected for a number of reasons. Frequently, young children do not receive vitamin-A rich foods such as yellow and dark green fruits and vegetables in addition to the normal starchy diet. Butter or other dietary fats which would assist in metabolizing vitamin A are also lacking in the diet. Often cultural practices of child feeding result in vitamin A deficiency. For example, while breastfeeding usually provides a baby with adequate vitamin A, substitute formulas, watered-down formulas, and inappropriate weaning foods may result in vitamin A deficient diets.

Furthermore, infections increase the need for vitamin A at the same time they reduce absorption of nutrients. For example, there appears to be a strong link between xerophthalmia, protein-energy malnutrition, and diarrhea.

The lack of awareness of the true magnitude of the problem, according to Dr. John McKigney of the Agency for International Development, is a result of the following factors:

1. Affected children are primarily from poor families, who often live far from health facilities.
2. The susceptible age group children, aged 1 through 5, demonstrate the symptoms of eye lesions slowly and inconspicuously.
3. Children affected frequently suffer other health and nutrition problems such as malnutrition, measles, and diarrhea, which receive more attention than the vitamin A deficiency.
4. Many health and nutrition professionals are not trained to diagnose vitamin A deficiency eye disease.

The consequences

Xerophthalmia, also known as nutritional blindness, is the leading cause of preventable blindness in children. It is caused by an insufficiency of vitamin A in the diet and is frequently associated with other forms of malnutrition, infection, diarrhea, and a high rate of mortality.

The World Health Organization estimates that 5 million preschool age children in Asia alone develop xerophthalmia every year, and that 250,000 Asian children are blinded by the disease each year.

Blindness in less developed countries is a problem of immense costs, not only in terms of human suffering, but also in terms of social and economic losses. Families of blind persons must assume the cost of feeding, clothing, and sheltering the blind person, as well as sacrificing a family member with vision to care for the one who is blind. Thus, the economic loss of blindness is equal to the productivity of two or three persons.

While blindness is the most dramatic result of vitamin A deficiency, it is one of the last symptoms of deficiency. Before blindness occurs, lack of vitamin A leads to decreased appetite and stunted growth in children. It also greatly increases the body's susceptibility to disease. There is mounting evidence, described later in this report, that vitamin A deficiency is clearly linked to increased illness and death rates in children worldwide. Dr. Alfred Sommer, Director of the Johns Hopkins Center for Preventive Ophthalmology, estimates that 20 to 35 percent of all childhood mortality may be related to vitamin A deficiency.

In the more advanced stages of vitamin A deficiency, the eyes are impaired. Signs of night blindness are the first warnings of vitamin A deficiency. Children in less developed countries who stumble at twilight, or who cannot find their food at the evening meal, may be suffering from vitamin A deficiency. As the deficiency continues and becomes more pronounced, spots, known as "Bitot's spots," appear on the white conjunctiva of the eye. With advanced deficiency the degeneration of the eye continues, eventually leading to blindness.

Much work has been done in recent years on the detection, treatment, and prevention of xerophthalmia, or vitamin A blindness. The International Vitamin A Consultative Group (IVACG) and the World Health Organization (WHO) have developed a classification

system which assists health care workers to detect and treat the problem before it results in blindness.

II. VITAMIN A DEFICIENCY—PREVENTION

There are several strategies which have been identified by the international community as appropriate for vitamin A intervention programs. Different strategies may be appropriate depending on the economic and cultural factors prevailing in countries and regions with high levels of vitamin A deficiency. Following is a discussion of those strategies currently in use.

High-level doses

The most widely practiced short-term intervention measure in regions where vitamin A deficiency is endemic is periodic oral delivery of high-dose vitamin A to the most vulnerable population groups. The dose is usually 200,000 International Units (IV) of vitamin A, delivered every 6 months to children aged 1 through 5.

All countries except India use an oral gelatin capsule provided by the United Nations Children's Fund (UNICEF) containing both vitamin A and vitamin E. India produces and uses an oil solution. Such distribution programs generally reach up to 60 to 80 percent of the target group. One drawback of these programs is that those children most at risk of vitamin A deficiency are frequently not reached because of inaccessibility or lack of awareness.

The first trials of this approach were carried out in Guatemala, Jordan, and India. Large-scale programs are being conducted in India, Bangladesh, Indonesia, Haiti, Philippines, Sri Lanka, El Salvador, Thailand, Tanzania, and Malawi.

Large dose programs appear to have significant impact in reducing the prevalence of blindness. During 8 years of capsule distribution in Bangladesh, the prevalence of blindness in children 0--6 years of age was reduced from 27 per 10,000 (0.276 percent) to less than 4 per 10,000 (0.038 percent).

Only recently have large-scale field trials of program effectiveness been completed. A large research project, funded by AID and conducted by the International Center for Epidemiologic and Preventive Ophthalmology, Johns Hopkins University, the Ministry of Health of Indonesia, and Helen Keller International, an American private voluntary organization, has provided dramatic evidence that vitamin A is intimately linked to child health and survival in less-developed countries.

Thirty thousand children in 450 villages were randomly assigned to participate in a vitamin A supplementation program. Each assigned child was to receive a large dose of vitamin A therapy once every 6 months. The Government of Indonesia had planned such a vitamin A distribution program, but could only cover one-half of the villages with the funds available. Therefore, villages were randomly selected to participate in the program, and were compared with neighboring villages.

Before beginning the program, all children were examined and, if they demonstrated evidence of vitamin A deficiency, were treated. All children were reexamined 1 year later. The results were startling.

Mortality rates among children under 6 years of age living in treated and untreated villages differed by over 30 percent. In other words, vitamin A supplementation reduced childhood mortality rates by approximately 25 percent in the under 6 population. An even more revealing comparison is the mortality rate among children 1 to 5 years of age in the two study populations, as children below 1 year of age were not eligible for receiving a vitamin A capsule. In this age group, mortality rates among nonsupplemented villages were 50 percent higher than they were in program villages. The cost was an estimated 22 cents per delivered dose. The annual cost of delivering vitamin A twice a year to 30,000 children would be $13,200.

In 1985, AID will fund several replication studies to determine the applicability of these findings to other geographic locations. These studies are planned for evaluation of programs in Bangladesh, Philippines, India, and Zambia. The funding for these studies was made available by the increased appropriations for nutrition assistance and primary health care which Select Committee members pressed for in 1984.

Fortification

Fortification of foods with specific nutrients to prevent deficiencies was first tried by adding cod liver oil concentrate to margarine in Denmark during World War I. This followed an epidemic of xerophthalmia which resulted from the replacement of butter with margarine in the Danish diet. When fortification successfully stopped the epidemic, vitamin A fortification of margarine became routine in many developed countries. Margarine is also fortified in several developing nations, including Brazil, Colombia, Chile, Mexico, Peru, the Philippines, and Turkey.

Widespread fortification of food aid with vitamin A first occurred when the U.S. Government began to fortify nonfat dry milk for its Public Law 480 food donation program. All nonfat milk from the U.S. Government now distributed through international food donation programs is fortified. Vitamin A fortification is also routine for blended foods made available through Public Law 480 programs. Furthermore, many locally produced blended foods for children are fortified. While it is unclear whether such fortification programs reach the children most at risk of vitamin A deficiency, it is almost certain that vitamin A fortification has prevented vitamin A deficient blindness in less developed countries.

Fortification of a commonly consumed food is an effective means of improving vitamin A intake. However, there are many factors which can impede fortification programs. The food to be fortified should be widely consumed by the population at risk of vitamin A deficiency, it should be centrally processed so that fortification is universal in the food supply, and there should be a reasonable assurance that neither an inadequate or excessive amount of vitamin A will be eaten, given normal consumption patterns of the chosen food within the specified area. Other factors to be considered are the acceptability of the final product after fortification and the economic feasibility of fortification.

Research on vitamin A fortification in Central America led to legislation in four countries—Costa Rica, Guatemala, Honduras,

and Panama—mandating that all centrally processed sugar for home consumption be fortified with vitamin A. Prior to fortification, dietary studies conducted by the Institute of Nutrition of Central America and Panama (INCAP) indicated that 83 percent of Guatemalan families had diets that were severely inadequate in vitamin A, and that the Guatemalan children consumed 33 grams of sugar daily.

The effect of fortification was studied over a 2-year period. Studies conducted in 12 representative rural communities and 30 families randomly selected in each demonstrated that blood indicators of vitamin A (serum retinol) significantly increased, and that the number of children with deficient values significantly decreased. The cost per person in the country was 7 cents in 1976. The other countries involved did not conduct such extensive analyses. However, data from Costa Rica indicated that the extent of vitamin A deficiency among children dropped from 32.5 percent in 1966 to 2.3 percent in 1978 after sugar fortification had been in effect for 3 years.

In the Philippines, the food chosen for fortification was monosodium glutamate (MSG), a flavor enhancer. MSG was chosen because it is added to foods regularly fed to young children. Ninety-five percent of families used it regularly, and most families consumed 2 to 3 small packets of MSG daily. Most importantly, 98 percent of MSG was produced by one manufacturer. Other considerations were that MSG can be fortified without reducing its flavor-enhancing properties or significantly increasing the cost of the product.

Several problems plagued the project. The fortified MSG product was a different color, and "caked" in the package, making it less desirable than the unfortified MSG. A new form of vitamin A concentrate proved to be less potent than anticipated, reducing the effectiveness of the fortification level. And finally, opposition from some members of the medical community in the Philippines, concerned about MSG toxicity, led to public concern on the effectiveness of this approach.

The Government of Indonesia is currently working closely with Helen Keller International to determine the effectiveness of fortifying MSG with vitamin A in Indonesia. The Indonesian investigators are working to avoid the difficulties encountered in the Philippines, and hope to determine whether fortification, at a cost of 6 cents per child served per year, is as effective as the ongoing capsule distribution program, which costs 44 cents per child served annually.

Production of vitamin A-rich foods

The United Nations Food and Agriculture Organization (FAO) has shown that vegetable products are the main dietary source of vitamin A in most countries where vitamin A deficiency is prevalent. Vegetables provide 86 percent of dietary vitamin A in Africa and Asia, 65 percent in the Near East, and 53 percent in Latin America. Vitamin A deficiency is exacerbated by the fact that those most vulnerable, young children from 0–6 years of age, are frequently not fed vitamin A-rich vegetables as a normal part of the diet. Therefore, promotion of production and consumption of

low-cost vegetables and fruits which contain vitamin A is a viable mechanism for enhancing dietary sufficiency of the vitamin.

Several factors inhibit promotion of food production based on nutritional impact. Most research has been geared toward market considerations, such as high yielding varieties, and standardized colors and shapes, rather than nutritive content. Promotion of vitamin A-rich foods also has often encouraged use of foods available in developed countries rather than traditional food sources. Very little research on local food production and food consumption by individual families has been undertaken.

There are several useful publications available. Tropical Leaf Vegetables in Human Nutrition lists a large number of locally available foods which could prevent vitamin A deficiency in tropical areas around the world. The senior author, Dr. Oomen, has worked for years in Indonesia to promote the use of local vegetables in family diets. In India, a blindness prevention project of the government Ministry of Health and the British Royal Commonwealth Society for the Blind encourages the consumption of vegetables by young children in low-income Indian families. UNICEF has supported the promotion of home and school gardens in developing countries for many years as a means to improve the nutritional content of family diets.

The Asian Vegetable Research and Development Center (AVRDC) is supported in part by AID, and promotes home gardens in Asian countries. AVRDC's outreach program works with government officials to distribute seeds and promote gardens through extension programs. Vegetables which are good sources of vitamin A have a high priority in garden projects throughout Asia, given the importance of vitamin A deficiency in that region.

Recent work in certain African countries has pointed to the encouragement of local growing, preservation and consumption of vitamin A-rich foods as a priority activity there. AID currently has vitamin A projects in Malawi and Zambia.

Nutrition education

Nutrition education is obviously needed when vitamin A-rich foods are readily available, and yet vitamin A deficiency diseases are still prevalent. In some countries, placing special emphasis on vitamin A within other more broadly based health and nutrition activities is sufficient. In others, it may be necessary to have a separate nutrition education effort specifically addressed to vitamin A. Because of these differing needs, AID and the major PVO's active in vitamin A programs have developed training aids, nutrition education materials, and a field guide for detecting vitamin A deficiency xerophthalmia. The UNICEF Home Gardens Handbook places particular emphasis on vitamin A-rich foods for gardens. The International Vitamin A Consultative Group has published a series of monographs for use by professionals around the world to inform and stimulate action toward preventing vitamin A deficiency.

Some national activities include:

A flip book distributed to 13,000 primary health workers in Bangladesh;

Emphasis on vitamin A programs in the medical, health and nutritional personnel curricula in Haiti;

Collaboration of the Directorates of Health, Education and Nutrition with the Ministry of Health on nutrition education in Indonesia; and

Vitamin A newsletters from the National Nutrition Council and the Nutrition Center of the Philippines.

Public health

Public health measures which improve the environment and reduce conditions leading to increased need of vitamin A will also reduce vitamin A deficiency. Because vitamin A deficiency is closely associated with measles, immunization programs against measles could reduce levels of vitamin A deficiency. Similarly, water and sanitation programs which reduce the incidence of diarrheal and infectious diseases should have a similar and associated impact on vitamin A deficiency diseases.

III. VITAMIN A DEFICIENCY—INTERVENTION

In testimony before the Select Committee on Hunger on May 16, 1985, John Costello of Helen Keller International described ongoing programs of vitamin A supplementation and opportunities for expanded efforts. Costello described an extraordinary effort to distribute vitamin A supplements to the victims of the Ethiopian famine.

Emergency measures

Early in 1985 investigators discovered that rates of nutritional blindness in feeding camps in Ethiopia and Sudan were among the highest ever recorded—up to 10 percent of the children had advanced symptoms. Many were already irreversibly blind.

Helen Keller International sought and obtained from Hoffman-LaRoche & Co., Ltd., a pharmaceutical company, the donation of 5 million doses of vitamin A to cover immediate and future needs. Pharmacaps, Inc., of Elizabeth, NJ, packaged the vitamin A concentrate into 2 million capsules for immediate use. SETCO, Inc., of Cranbury, NJ, gave plastic bottles, and Teshcon Corp. of Westbury, NY, packed and prepared the capsules. Catholic Relief Services and the United Nations High Commissioner for Refugees helped with shipping arrangements. Among the agencies that are delivering the vitamin A in Sudan and Ethiopia are Catholic Relief Services, Christian Relief and Development Association, Medicins sans Frontieres (Doctors Without Borders), Oxfam-U.S., and Save the Children-UK.

On-going measures

In addition to these immediate and emergency needs for vitamin A programs, Helen Keller International and other private voluntary organizations are involved in ongoing programs. Fourteen organizations and 18 countries have ongoing or planned programs to prevent or treat vitamin A deficiency. Helen Keller International has provided service in over 80 countries. The International Eye Foundation provides training in blindness prevention in many countries. They are active in Kenya, Malawi, Guinea, Egypt, Puerto Rico, Barbados, Grenada and Saint Lucia, and the Dominican Republic.

Other important centers for research and program development for blindness prevention activities include the Asian Foundation for the Prevention of Blindness in Hong Kong, Foresight in Australia, the Canadian National Institute for the Blind in Toronto, Canada, the National Eye Institute in Bethesda, Maryland, the International Center for Epidemiologic and Preventive Ophthalmology in Balitmore, Maryland, and the International Vitamin A Consultative Group in Washington, D.C.

In 1976 AID, WHO, and the United Nations Children's Fund (UNICEF) created the International Vitamin A Consultative Group (IVACG) to coordinate global efforts to fight nutritional blindness. Funded largely by AID, IVACG is composed of scientists and representatives of governments, international donors, and private voluntary agenices.

The Agency for International Development (AID) has played a key role in the world efforts in vitamin A nutrition. Since 1974, AID has spent $4.5 million to help train people in developing countries to recognize, treat and prevent vitamin A deficiency. Over 20 countries have been assisted in developing programs, and 13 have been assisted in beginning prevention programs.

Dr. John McKigney, vitamin A specialist at AID, estimates that such programs save 100,000 children a year from a life of blindness. Hundred of thousands more may be saved from preventable deaths due to measles and other diarrheal and respiratory diseases closely associated with vitamin A deficiency. (AID Horizons, Spring 1985)

Funding

Funding for vitamin A activities through AID has been limited. From 1975 to 1984 only $4.5 million was allocated to vitamin A activities. New activities will be possible this year only because Congress appropriated an additional $10 million for nutrition assistance in the fiscal year 1985 legislation. Of that total, $3 million is expected to be obligated for vitamin A activities. An additional $2 million in other accounts is also used for vitamin A activities.

However, the fiscal year 1986 budget request for AID contains only minimal funding to continue this expanded effort. The funding levels requested for health and nutrition in fiscal year 1986 are over $100 million below what Congress appropriated in fiscal year 1985, and there is only $575,000 allocated for vitamin A activities in the Office of Nutrition budget.

John Costello of Helen Keller International stated in his May 16, 1985 testimony: "I can tell you, on tne basis of recent visits to several developing countries, that USAID mission directors state that they are extremely short of funds for health and nutrition programs and of technical experts in the health field."

SUMMARY

New evidence on the role of vitamin A supplementation in greatly reducing childhood illness and death rates has stimulated congressional interest and discussion.

In 1984, Members of the Select Committee on Hunger worked for the enactment of legislation to significantly increase funding for health and nutrition assistance programs through the Agency for

International Development. Because of that increased funding, it will be possible in 1985 to enhance ongoing programs of basic health and nutrition, as well as to create innovative programs in selected countries with high rates of infant and child mortality. Work on vitamin A is in the forefront of this effort.

Data in this report indicates that vitamin A intervention program, that is, campaigns administering large oral doses of vitamin A to young children, are inexpensive, practical to administer, and cost-effective in terms of health and human productivity, reducing both vitamin A blindness and overall rates of child death and disease.

In addition to programs delivering "golden bullets" doses, a variety of activities promote foods which are either good natural sources of vitamin A or fortified with vitamin A. Such foods as nonfat dry milk, cornmeal, and wheat flour distributed through the U.S. Food for Peace Program are fortified with vitamin A. Many countries where vitamin A deficiency is a known problem are working to develop staple foods and local weaning foods which are vitamin A fortified.

For the long term, nutrition education, expanded public health efforts, and promotion of gardening and agricultural extension projects emphasizing dietary sources of vitamin A can help to assure the eradication of vitamin A blindness throughout the world.

APPENDIX

Review of Literature Linking Vitamin A Deficiency to Child Mortality

(By Daniel L. Kraushaar, Sc.D., Helen Keller International)

STATEMENT OF THE PROBLEM

Blinding malnutrition (xerophthalmia), brought on by vitamin A deficiency, affects about 500,000 pre-school-age children in Bangladesh, India, Indonesia and the Philippines annually. The incidence of milder forms of xerophthalmia may be as much as ten times higher (1). In a national xerophthalmia prevalence survey conducted jointly by The Government of Indonesia's Department of Health, Directorate of Nutrition, and Helen Keller International, the prevalence of xerophthalmia corneal involvement for rural Indonesia in 1979 was 2.7 per thousand (2), indicating that well over 60,000 new cases (in children 0–6 years of age) of corneal xerophthalmia occur in Indonesia each year, and prevalence rates for xerophthalmia in well over half of Indonesia's provinces exceeding by as much as 40 times the World Health Organization's standards for what constitutes a public health problem.

Most recent programmatic efforts to reduce vitamin A deficiency in Indonesia have been based on Vitamin A supplementation, which is now seen as a routine part of many comprehensive nutritional programs worldwide. In Indonesia, vitamin A supplementation is a routine component of the national Family Nutrition Intervention Programme (UPGK), to be implemented in all villages in the country by the end of this five year development plan (PELITA IV) 1984/85–1988/89).

Vitamin A deficiency may have a much larger role to play in reducing childhood morbidity and mortality than simply reducing the prevalence of nutritional blindness (xerophthalmia). Evidence from studies conducted over the past 40 years, and more recent field epidemiological studies in Indonesia, indicate that vitamin A deficiency may be heavily implicated in childhood morbidity and mortality.

HYPOVITAMINOSIS A AND INFECTION

No nutritional deficiency is more consistently synergistic with infections and parasitic disease than that of vitamin A. Some authors hypothesize that hypovitaminosis A renders people more prone to infection and life-threatening diseases. When an inadequate amount of vitamin A is consumed, the body does not have a sufficient level of the nutritient for optimal cell formation and function. Depending upon the degree of the deficiency, mild or severe biochemical and clinical signs will develop, a condition termed hypovitaminosis A. Hypovitaminosis A normally indicated by clinical changes in the eyes. Mild forms of hypovitaminosis A lead to conditions of night blindness (X1B), with more severe hypovitaminosis A eventually causing loss of sight (X2/X3). Although there is little evidence from current epidemiological field studies of the causative vitamin A deficiency-infection link in man, a number of clinical and pathophysiological studies indicate that such a relationship exists. Most of the studies reviewed relate to the effect of gastroenteritis and other infections on the absorption of vitamin A; assuming that the relationship is unidirectional, i.e., infection reduces vitamin A availability (tables 1,2). Few studies have attempted to assess the extent of the relationship in the opposite direction, i.e., vitamin A as a cause or contributor to infection. In acute infectious diseases, plasma vitamin A levels usually are depressed and transport mechanisms become less efficient. Hypoprotenemia, protein-calorie, malnutrition, stress, wounds, chronic infections and parasitic infections all serve to decrease the utilization of vitamin A, the result being a higher incidence and prevalence of blinding malnutrition or xerophthalmia.

One of the most elaborate studies relating nutritional status and morbidity was that conducted by The Johns Hopkins University, School of Hygiene and Public

Health in the Naranqwal, India (3). The Narangwal project's main purpose was to determine the effects of differential child care services—nutrition supplementation and infectious disease control singly or in combination—on parameters of child health. They categorized children into two groups: malnourished and well nourished. Parameters of nutritional status, such as anthropometrical measurements, biochemistry, food intake and socioeconomic level were then used to examine some of the conditions leading to morbidity. Data were analyzed through tests of the null hypothesis using chi square or student's "t" tests on proportions or sample means respectively, making pairwise comparisons on these parameters between these two groups. In addition, discriminant analysis on related variables was used to determine, from among all variables examined, those that might prove important in the etiology of malnutrition. Vitamin A intake was one variable used.

Vitamin A intake was significantly lower in the underweight group as a whole as well as in different age groups. For dietary intake variables, vitamin A was significantly different between the malnourished and wellnourished children. Using stepwise discriminant analysis, vitamin A, with the highest level of significance (largest F value), proved the most discriminating of all variables in differentiating the two groups. The two groups were later compared in relation to their level of morbidity, with the wellnourished having fewer health problems and an overall lower mortality, as would be expected. The authors caution, however, that vitamin A as a variable in the analysis, may have acted as a proxy variables for a combination of other variables that tend to be associated with malnutrition.

The progress from hypo- to hypervitaminosis A can be seen in figure 1. This figure indicates that an inadequate intake of vitamin A results in insufficient levels of the nutrient for optimal cell formation and functions. Depending upon the degree of insufficiency, mild or severe biochemical and clinical signs will develop. Severe vitamin A deficiency leads to irreversible loss of eyesight together with a (hypothesized) greater susceptibility to infections and other accompanying nutritional deficiencies; the condition frequently leads to death.

The interaction between vitamin A deficiency and infection can either be characterized as "antagonistic" or "synergistic" (4). An antagonistic response to vitamin A deficiency would be one in which a deficiency of vitamin A leads to a decrease in the particular host's problem. Synergism, on the other hand, refers to an increase in the problem with a decrease in the host's level of vitamin A. This synergistic relationship between the deficient vitamin and infection has been clearly shown in the literature.

There are several patterns of interaction between vitamin A deficiency and infection (4). It is possible that the vitamin A-infection link can be the result of the genetic constitution of the host, i.e., natural resistance is high or low, or it may be due to specific host factors such as sex or age. For example, xerophthalmia is a predominantly a disease of the young. Thirdly, most specific vitamin deficiencies, vitamin A included, interfere with antibody production in experimental animals. Some studies have shown that vitamin A deficiency has had a depressing effect on antibody response and pteroyl-glutamic acid deficiency. This effect is presumably due to interference with protein synthesis (5).

Fourth, it is possible that nutritional deficiencies can interfere with antibody response; in some diseases and in some hosts this could result in some synergism with the infectious agent. Reduced phagocytic activity can also be the cause of the synergism. In vitamin A deficiency, phagocytic activity is depressed in both rats and humans.

Another possible reason for the synergism is that most commonly attributed to vitamin A deficiency. Altered tissue integrity of the epithelial tissues could influence infection through a variety of mechanisms, not the least of which would be increased permeability, reduction or absence of mucous secretions, and loss of ciliated epithelium in the respiratory tract. For example, salmonella penetration to the viscera could be enhanced leading to increasing frequency of diarrhea.

Finally, interference with nonspecific protective substances, nonspecific destruction of bacterial toxins and alterations in intestinal flora could also be implicated.

Perla (6) showed that lab animals maintained on diets deficient in vitamin A exhibit increased susceptibility to naturally acquired and specifically induced infections. Some or all of the results of other studies have indicated that vitamin A deficiency leads to impaired antibody responses to specific immunizations [Ludovici (7), Krushnann (8)] and impaired phagocytosis [Perla (6)]. Some, or all, of these changes may favour increased susceptibility to infections. A study conducted by Zile (9) also demonstrated delayed migration of intestinal mucosal cells in vitamin A deprived rats. The authors suggested that the vitamin A deficient animals may have an im-

paired ability to withstand various stresses because of the delayed renewal and elimination of abnormal or diseased cells.

In addition to the above, there is evidence that large doses of vitamin A can induce profound effects on the immunological system. Several authors have described enhanced antibody responses to specific antigens after the administration of varying doses of vitamin A to laboratory animals. It has also been shown that vitamin A can also have a positive influence on cell-mediated immunity.

Kenneth Brown, also from Johns Hopkins University, researched the interaction between gastroenteritis and vitamin A deficiency (10). While Brown states that infections can reduce the absorption of vitamin A and therefore gastroenteritis is implicated in xerophthalmia, it has been speculated that vitamin A deficiency may, in fact, predispose an individual to infections, including gastroenteritis; but the data in support of that contention are scanty.

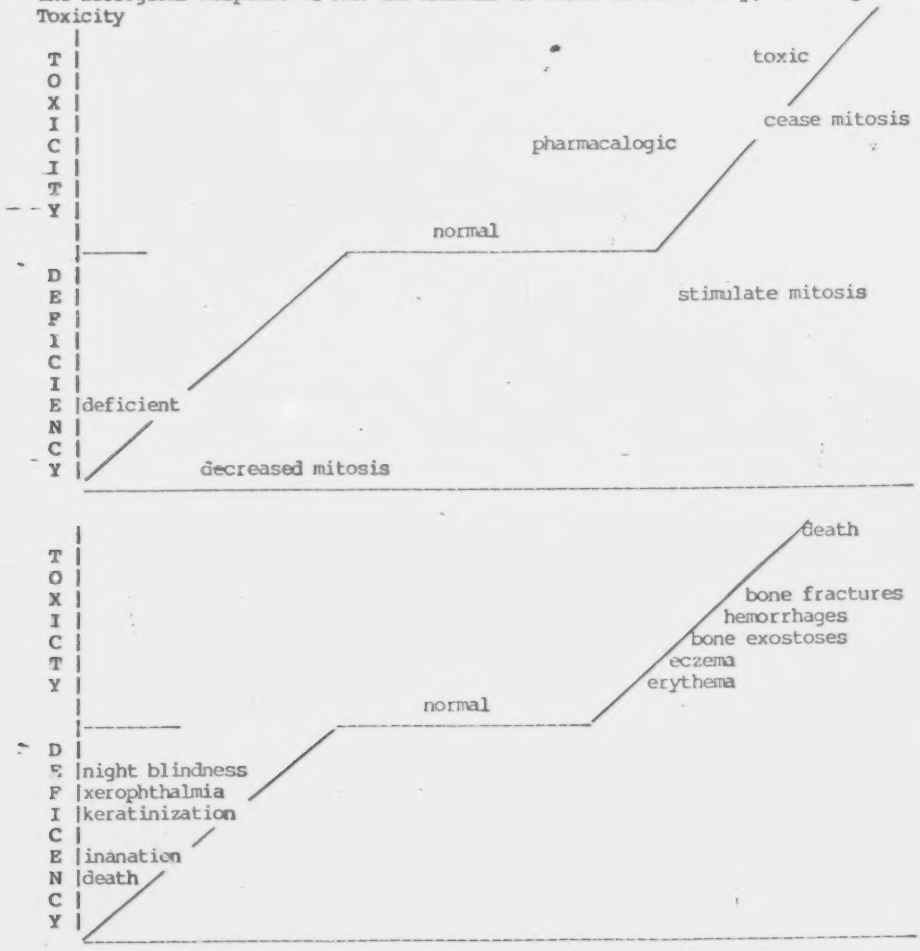
Although many studies have shown a high correlation between presence of xerophthalmia and some acute or chronic infections especially dysentery, gastroenteritic and measles as well as a variety of infectious diseases, the association is not surprising. Both conditions derive from poverty, unsanitary conditions, poor nutritional status, and the like. The causal interaction, however, is not easily determined. For example, both xerophthalmia and gastroenteritis have the highest incidence during the preschool years.

In 1965, a study conducted by Brown (11) of children with xerophthalmia who were hospitalized with severe PCM showed insignificant differences in either clinically defined diarrhea or specific enteric infections. These findings were different from those of McLaren (12) who reported that mortality in patients with xerophthalmia and PCM was significantly greater than in those with PCM alone.

Nutrition influences infection in at least four ways. According to Scrimshaw, et al, (4), nutritional deficiencies determine the progress of infection either through action on the host to facilitate initial invasion of the infectious agent; through an effect on the agent once established in the tissues; through favoring secondary infections; or by retarding convalescence after infection. Most of the literature does not differentiate these four possible means of interaction and it is unclear where vitamin A deficiency enters into this process.

figure 1

The Logarithmic Plot of Vitamin A Intake as a Function of the Biological Response of Man and Animals in Terms of Deficiency, Normalcy and Toxicity



The scheme at the top illustrates the response of a typical mucous epithelium, but is probably applicable to other undifferentiated blast-cell populations as well. The bottom curve indicates the clinical manifestations resulting from the altered cell function in deficiency and toxicity of vitamin A.

source: International Vitamin A Consultative Group (IVACG) The Safe Use of Vitamin A, 1980

TABLE 1.—HYPOTHESIZED CAUSES OF VITAMIN A—INFECTION SYNERGISM

1. Genetic constitution of host.
2. Natural resistance of host.
3. Age of host (very low or high increases synergism).
4. Vitamin A deficiency interferes with antibody production.
5. Vitamin A deficiency decreases protein synthesis.
6. Vitamin A deficiency decreases cell mediated immunity.
7. Vitamin A deficiency decreases phagocytic activity.
8. Vitamin A deficiency alters tissue integrity leading to decreased mucous secretion and reduction of ciliated epithelium.
9. Vitamin A deficiency interferes with non-specific protective substances.
10. Vitamin A deficiency reduces intestinal flora and destroys bacterial toxins resident in man.

PATTERNS OF INTERACTION WITH SPECIFIC INFECTIONS

The following studies have been classed as indicating synergism, antagonism or no effect. The tables have been taken from a review of the literature conducted by Scrimshaw, et al. (4), but only those references and results involving vitamin A have been used for this paper.

Bacterial infections

Table 2 indicates that the vitamin A-bacterial infection link is almost purely synergistic in nature. Although multiple deficiencies are most common in humans, these studies indicate that vitamin A deficiency is implicated in increased risk of pneumonia, tuberculosis, salmonella and other bacteria, bacillary dysentery and other severe infections. Monkeys on a diet deficient in vitamins A, B, C and an mal protein had chronic diarrhea typical of bacillary dysentery. McKenzie reported similar findings in East Africa laborers. Table 4 also indicates that children and animals on vitamin A deficient diets frequently develop spontaneous infections.

Viral infections

Both antagonism and synergism have been found in animal studies. Although only one of the studies specifically addressed vitamin A deficiency and viral diseases (resulting in a synergistic effect), the majority of the studies with multiple deficiencies indicated an antagonistic effect (table 3). In general, viruses show more specificity in their interactions with hypovitaminosis A.

Rickettsiae

All studies reviewed by Scrimshaw, et al, (4) indicated a synergistic relationship between vitamin A deficiency and rickettsial diseases. Specific vitamin A deficiency was reported in only two studies (13) indicating a synergistic relationship between vitamin A deficiency and typhus.

Helminths

Although the majority of the studies showing vitamin A or multiple vitamin deficiencies indicated a synergistic relationship with helminth infections, there were two examples where there was no interaction. Scrimshaw points out that helminth infections are generally more serious in malnourished hosts (table 4).

Protozoa

Only one study specifically looked at the vitamin A-protozoal infection link and indicated a synergistic relationship between vitamin A and B deficiency and coccidiosis (4). Multiple vitamin deficiencies indicate a mixed relationship, with both synergistic as well as antagonistic relationships observed. Regardless of these animal studies, several sources have indicated that inadequate diets can precipitate amoebiasis (15–16).

TABLE 2.—EFFECT OF VITAMIN A DEFICIENCY ON BACTERIAL INFECTIONS

Host	Deficiency	Agent	Action	Reference
Guinea pig	Multiple	Pneumonia	Synergistic	17
Rat	Vitamin A +	TB	No effect	18
Mouse	Multiple	Salmonella and 4 others	Synergistic	19
Do	do	Salmonella	do	20
Human	Vitamins A,C	TB	do	21

TABLE 2.—EFFECT OF VITAMIN A DEFICIENCY ON BACTERIAL INFECTIONS—Continued

Host	Deficiency	Agent	Action	Reference
Monkey	Vitamins A,C,B and protein	Bacillary dysentery	do	22
Rat	Vitamin A	Spontaneous infections	do	23–26
Infant	do	Severe infections	do	27
Do	do	do	do	28
Rat	do	Salmonella	do	29
Mouse	do	TB	do	30
Dog	do	Spirochetes	do	31
Guinea pig	do	Diphtheria tetanus	do	32
Rat	Vitamins A,D	Tetanus typhoid	do	33
Sheep	do	Lamb dysentery	do	34
Rat	Vitamin A	Saprophytic bacteria	do	35
Monkey	Vitamins A,B	Septicemia	do	36

Source: Scrimshaw, Nevin S., et al, "Interactions of Nutrition and Infection." The American Journal of the Medical Sciences, vol. 237, No. 3, March 1959.

TABLE 3.—EFFECT OF VITAMIN A DEFICIENCY ON VIRAL INFECTIONS

Host	Deficiency	Agent	Action	Reference
Cotton rat	Vitamin A	Poliomyelitis	Synergistic	37
African Negro	Multiple	Hepatitis	do	38–39
Monkey, mouse	do	Yellow fever	do	40
Monkey	do	Influenza	do	41

Source: Scrimshaw, Nevin S., et al., "Interactions of Nutrition and Infection." The American Journal of the Medical Sciences, vol. 237, No. 3, March 1959.

TABLE 4.—EFFECT OF VITAMIN A DEFICIENCY ON HELMINTH INFECTIONS

Host	Deficiency	Agent	Action	Reference
Chicken	Vitamin A	Ascaris galli	Synergistic	42
Dog	do	Toxicara canis	do	43
Rat	do	Strongyloides ratti	do	44
Do	do	Schistosoma mansoni	do	45
Do	do	Trichinella spiralis	do	46
Do	do	Parascaris equorum	do	47

Source: Scrimshaw, Nevin S., et al, "Interactions of Nutrition and Infection." The American Journal of the Medical Sciences, vol. 237, No. 3, March 1959.

Hodges (48) addressed the causal relationship between vitamin A and clinical problems in some depth. The clinical significance of deficiencies in vitamin A in adults is different from children, according to Hodges, but the underlying mechanisms seem to be the same. Experiments with adult subjects showed that when fed a diet deficient in vitamin A, adult young men experienced anemia, impaired colour vision, derangements of taste and smell and loss of vestibulary balance. Based on these studies and his personal observations in S.E. Asia, Hodges concludes that vitamin A is "necessary for the anatomical and physiological health of many and perhaps all epithelial cells". In addition, he adds, "it involves the structure of the skeleton, reproductive systems, avoidance of neoplasia and even survival itself." Referencing studies of immature animals, Hodges recounts that these animals fed a diet deficient in vitamin A showed stunting (low height for weight).

Hodges also believes that hypovitaminosis A is closely related to anemia. Hodges states that deficiency of vitamin A causes a reduction in serum iron concentrations and favoured deposition or iron in both liver and spleen. A number of researchers, however, have discounted this relationship (49).

In summary, evidence obtained from laboratory and human studies indicates that infections can reduce vitamin A absorption and utilization. In addition, some experiments have indicated that there may be an increased susceptibility to infections in the vitamin A deprived individual or animal. Even with this potential link, many conclude as Brown does, that "At present, it appears that the most practical and

effective way of preventing xerophthalmia (vitamin A deficiency is by increasing the intake of Vitamin A, since the prevention of gastroenteritis and malabsorption is not yet technically feasible in many of the poorest countries." (5) He and others overlook, in the end, the question of whether decreased vitamin A leads to increased risk of morbidity and mortality in a causal sense and whether vitamin A intake can indeed be a cheap and effective solution to overcoming some common causes of childhood morbidity.

CORRELATES OF VITAMIN A DEFICIENCY

Studies conducted in Indonesia by the Department of Health, Helen Keller International and Johns Hopkins University provide information as to the correlates of vitamin A deficiency, clarifying the setting in which vitamin A deficiency occurs and shows that proving the vitamin A deficiency-morbidity link in a field setting is extremely difficult (2).

Age

In Indonesia, vitamin A deficiency is essentially a disease of young children. 72% of individuals with Bitot's spots (mild xerophthalmia) and 96% with active corneal disease were under 6 years of age. This is not surprising in that protein-energy malnutrition and other common childhood infections occur in this age group and can exacerbate the effects of vitamin A deficiency. (table 5)

Sex

Bitot's spots were more prevalent in males than females, and was evident in every age group. Active corneal disease, however, was more prevalent in females. The study report postulates that "It is possible that although a greater proportion of males than females suffer from vitamin A deficiency, females deficient in vitamin A are more likely to be malnourished in general as well, and consequently the effect of their deficiency is more severe. Alternatively, for reasons poorly understood, males may be more likely to maintain their Bitot's spots long after the underlying vitamin A deficiency has been corrected."

Clustering

The presence of a case of clinical xerophthalmia suggests that the neighborhood is at particularly high risk of containing additional children with clinical or subclinical vitamin A deficiency. This portion of the study examined cases of xerophthalmia, their clinically normal controls matched for age, sex and neighborhood and a 5 per cent random subsample of the entire population. The levels among the abnormals were significantly lower than those among the controls, and in turn the levels among controls were significantly lower than those among the random sample. This indictes that clinically normal children (matched controls) living in the immediate neighborhood of xerophthalmic children are significantly more likely to be deficient in vitamin A than are clinically normal children who live farther away (random sample). This is not surprising since one may expect that the environmental, nutritional, economic and other conditions within neighborhoods would be nearly the same. This same clustering phenomenon was found for active corneal disease, corneal scars and Bitot's spots. In other words, the same conditions which lead to an initial case of disease are working on other members of the community who may or may not have an active case of xerophthalmia.

Nutritional and anthropometric status

Protein status.—Serum levels of albumin and transferrin among cases of corneal diseases were often depressed.

Edema.—29 percent of corneal cases had clinical edema and its prevalence increased with the severity of the disease, and in turn less prevalent in milder forms of the disease.

Weight for height.—Wasting, or low weight for height, was extremely common in the presence of active corneal disease. The severity of the wasting increased with the severity of corneal involvement. In paired analysis with matched controls, the matched control was more severely wasted than the abnormal in only three instances (n=32). The relative risk of corneal disease among children with a weight for height that was less versus equal or greater than 80 percent of standard was 35 to 1. Although active corneal disease was associated with wasting, the presence of Bitot's spots was not.

Height for age.—Height for age reflects long-term growth, which is affected by restrictions in both calories and protein, severe systemic illnesses and other problems. Diminished height for age is called stunting.

Active corneal cases were shorter than their paired matched controls. This clear stunting of cases was clearly statistically significant ($p<.01$). Based on these results it was clear that children with active corneal disease were not only wasted but also stunted. From these results, however, it was unclear whether wasting contributes to the manifestation of xerophthalmia, whether wasting merely indicates that children whose intake of vitamin A is especially low are likely to have an especially low intake of other nutrients as well, or whether severe vitamin A deficiency contributes directly to poor nutritional status.

Nonocular illness (excluding measles)

Diarrhea.—Among the 156 cases of active corneal disease, 7 percent ($n=11$) had gastroenteritis. This rate was almost twice as high as among their matched controls. Seventy two percent of all cases had a history of diarrhea (four or more stools a day) at some point during the previous month, as compared to 23 percent in their matched controls. The relative risk of corneal disease among individuals with and without a history of diarrhea during the previous months was 13 to 1.

If the association between both mild and severe xerophthalmia and a recent history of diarrhea is, in fact, causal, there are several possible explanations. Diarrhea may increase the risk of xerophthalmia or xerophthalmia may increase the risk of diarrhea. The fact that the association with diarrhea is greatest for the week immediately preceding the examination, when the vast majority of Bitot's spots surely were already present, suggests that xerophthalmia may have led to the diarrhea.

Worms.—Between one-fourth and one-third of the normals and abnormals had a history of passing worms during the preceding month. There seemed little association between xerophthalmia and passing of worms.

Respiratory tract disease.—Respiratory tract disease (fever plus cough or rales) was the most common condition accompanying corneal disease. Its prevalence was directly related to the severity of corneal involvement. Among cases with less severe corneal disease, the prevalence of respiratory tract disease was identical with that of their matched controls. It was unclear whether the severity of xerophthalmia and the accompanying malnutrition led to the respiratory tract disease among cases of corneal disease, or whether the combined effects of generalized or protein malnutrition and respiratory tract disease on the metabolism of vitamin A resulted in more severe xerophthalmia.

Measles

The report of the national prevalence study states (2):

"The role of measles in pediatric blindness is discussed separately for several reasons. First, in other cultures (most notably, Africa), measles rather than xerophthalmia is claimed to be the most important case of pediatric blindness by far, contrary to the experience in Asia in general and in Indonesia in particular. Second, despite these expectations, measles appears to account for a significant proportion of cases of pediatric blindness in Indonesia, especially of the severest, blinding type. Third, vitamin A deficiency seems to be the mechanism through which measles has its affect. And fourth, advances in immunization against measles suggest that measles prophylaxis may be an effective means of significantly reducing the problem of blinding xerophthalmia in Indonesia."

Of 162 active corneal cases, 6 (or 4 percent) had evidence of active measles. In all six cases, the disease was said to have appeared during the preceding one to three weeks, or after the onset of xerophthalmia. This prevalence was significantly higher than in milder forms of xerophthalmia. Although measles was more common among abnormals than matched controls in the paired analysis, the numbers were too small to be statistically significant. The relative risk of active corneal disease among those with and without a recent history of measles was 11 to 1. Although parents of 64 percent of all children with active corneal cases claimed that measles had preceded the onset of corneal disease by one to four weeks, it did not precede less severe forms of xerophthalmia.

Breast feeding

Those with xerophthalmia were less likely to be breast fed than their matched controls.

Diet

Xerophthalmia cases were less likely to include in their diets green leafy vegetables and carrots. Although two-thirds of the abnormals already consumed green leafy vegetables at least one a month, the frequency of consumptions and the quantity was significantly less.

VITAMIN A DEFICIENCY AND MORTALITY

Many international organizations recently have given recognition to the potential vitamin A-mortality link. The WHO's Subcommittee on Nutrition (21) states:

"Vitamin A deficiency is a widespread nutritional disorder with serious health implications for children in many developing countries. It is estimated that in Asia alone more than 10 million children are affected by vitamin A deficiency, and more than 1 million of these go blind every year. Only 30 per cent of these blind children survive."

Such general references can also be found in the literature pertaining solely to blindness. Sprague (51), stating that xerophthalmia usually occurs in a setting of malnutrition or infection, notes that the mortality associated with persons with severe vitamin A deficiency is high. Other authors have reported results such as this. In Jordan malnourished children with xerophthalmia had a four-fold increase in death rate over those with comparable malnutrition, but without eye lesions (52). In India, those who survived acute eye disease had a higher one-year mortality than age-matched controls (4).

In Indonesia, the first hint of the vitamin A-mortality link came in 1979 as a result of the national prevalence survey. The final report of the survey indicated that as many as 77 percent of the corneal cases died. Although the researchers recognized that this may have been higher than the true mortality rate, for a large portion of these deaths were undoubtedly related to the severe systemic illness and generalized malnutrition commonly accompanying xerophthalmia. Using a modified life table analysis, the overall mortality among children with corneal disease was 12.6 percent over a 14 month period. This varied, however, from 3.8 percent for children without severe protein-energy malnutrition to 25.7 percent for children with severe protein-energy malnutrition.

In a more specific look at this issue in Indonesia, Sommers, et al (2), using data from the Indonesia National Prevalence Survey conducted in 1978, looked into the relationship between vitamin A deficiency and mortality. An average of 3,481 preschool-age children were examined every 3 months for 18 months. The mortality rate among children with mild xerophthalmia (night blindness or Bitot spots which characterizes vitamin A deficiency) was on average 4 times the rate (and in some cases considerably more) among children without xerophthalmia. This relationship remained after stratification for respiratory disease, wasting, gastroenteritis, pedal oedema and childhood exanthems.

Sommer et al., found that children with mild xerophthalmia (night blindness and Bitot's spots), including those who were apparently otherwise well nourished and free from important systematic disease, had a mortality rate several times higher than that of the non-xerophthalmic peers. Furthermore the excessive mortality increased with the severity of the xerophthalmia.

In summary, the authors state:

"It is unlikely that this excess mortality is directly attributable to the presence of night blindness or Bitot's spots, although the former may reduce, to some extent, the child's ability to compete at the cooking pot with his better sighted peers. More likely it results, in part, from the systematic effects of impaired vitamin A metabolism, particularly those that are related to resistance to infection. Vitamin A deficiency results in keratinisation of the respiratory, gastroentistinal, and genitourinary tracts among others, thus increasing the risk of bacterial colonization and infection. It may also interfere with immune competence."

In addition, the mortality rate is compounded when other systemic infections such as respiratory tract infections or measles and with poor nutritional status leading to stunting and wasting. Tables 13 and 14 indicate that mortality increases in a linear fashion according to the degree of xerophthalmia (and presumably degree of vitamin A deficiency). The presence of wasting and respiratory tract infections further increases the mortality rates observed. Although these data further substantiate the vitamin A deficiency-mortality link, they do not offer insight into the cause-effect relationship.

In a more recent study in Aceh province, designed to conclusively study the effectiveness of periodic massive dosing of vitamin A in reducing xerophthalmia, this same relationship is being studied (53). Two intervention programmes were initiated in separate areas. They were:

(1) special vitamin A capsule distribution at six-month intervals to all preschool-age children by a village worker (UNIVAC), including distribution of vitamin A to all preschool children as part of the national family nutrition project (UPGK);

(2) administration of vitamin A capsule to all children with signs or symptoms of xerophthalmia upon examination (TARVAC).

Although not one of the original project goals, one of the researcher's interests was an assessment of the impact on child mortality of massive vitamin A dosing. Preliminary data indicate that the relative risk of mortality of preschool-age children in villages not receiving vitamin A was 1.3 compared to a relative risk of mortality of 1.0 in children in vitamin A distribution villages.

Age specific mortality rates in TARVAC and UNIVAC villages indicated that at all age groups from 0 to 60+ months the relative risk of mortality was greater in TARVAC villages than UNIVAC villages. This relationship peaked in the 24-35 month group. The children who died were found to have been much less likely to have received a vitamin A capsule.

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